natural course, that those tonsils which are removed with a full understanding of the immediate anatomy are entirely removed. Careful inspection of the fossae, and particularly the plica triangularis and the adjacent lymphoid tissue, is vitally important. The instruments used in a tonsillectomy are a matter of individual preference, but the fundamental thing of importance is a painstaking, nontraumatic, complete removal of the tonsils. A focus of infection is thereby eliminated, which is the real reason for removing the tonsils.

W. H. JOHNSTON, M.D. (1515 State Street, Santa Barbara).—We all acquire a technique for this operation after we have been in practice a few years, and I believe that we should continue to use the method which, in our hands, has given us the best results. Most of us try to do the complete operation described by Doctor Hunt, but I fear that we are not all getting the ideal end-results in 100 per cent of our cases. I have had the experience, many times, of completing what I thought was a perfect job, only to find a few months later a mass of lymphoid tissue at the lower part of the tonsillar fossae. I have also had the experience of doing a somewhat hasty operation and later finding that the end-result was perfect. We are overlooking something in the patient's make-up, and must remember that there are cases which we might call of the lymphatic type in which it seems impossible to do any type of operation that will insure against regrowth of lymphoid tissue at the lower pole. In this class we must look for some etiological factor, the discussion of which might go on indefinitely and does not belong under the heading of this paper. Some years ago French described an operation which he called "extended tonsillectomy"; it was quite similar to the one described by Doctor Hunt in reference to the lymphoid extension to the base of the tongue.

I agree with the essayist that many quoted statistics mean very little, because a considerable number of the operated cases retain remnants of infected lymphoid tissue in the tonsillar fossae. Most of us agree, I believe, that a piece of infected lymphoid tissue hemmed in with scars is much more harmful than was the original tonsil in many instances before an incomplete operation was performed.

I believe that we should all have a less casual attitude toward the tonsil operation, which now seems to come into the field of so many branches of the medical profession.

DRUG ERUPTIONS DUE TO THE BARBITURATES*

By FREDERICK G. NOVY, JR., M.D.
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DISCUSSION *by Harry E. Alderson, M.D., San Francisco; Stanley O. Chambers, M.D., Los Angeles; Philip K. Allen, M.D., San Diego.*

THE purpose of this paper is to discuss briefly the different types of cutaneous manifestations that may follow the use of the barbiturates.

Today the barbituric acid derivatives, of which there are a large number, have a widespread use in medicine for their sedative and hypnotic effects. Since these drugs were first introduced, eruptions of different types have been reported. Toxic skin reactions appear frequently following their administration, and should be constantly watched for. Menninger[1] states that about 2 per cent of the patients taking phenobarbital (luminal) develop some form of cutaneous intolerance. All of the barbiturates have been responsible for reactions, and there is no one form which is less likely to produce trouble. Phenobarbital and barbital (veronal), however, are the ones most frequently mentioned in the literature. This, I believe, is because of their more widespread use rather than that they are more toxic.

Why certain individuals react to these drugs is not fully understood. Undoubtedly the patient's general condition plays an important rôle. We see patients in good health who tolerate a drug, and later, when their general health has been impaired, a reaction to the same drug takes place. In these instances interference with the elimination of the drug could be a factor. A disturbance of the cardiorenal system would lead to retention of fluids and storage of the drug in the tissues. Other patients, probably the majority, have an idiosyncrasy to the drugs. This hypersensitivity can be explained in some patients who, having taken the drug some time in the past, have apparently become sensitized. Then later, upon administration of the same drug, a reaction occurs. This would account for the clinical fact that urticaria, a type of response that one would expect with hypersensitivity, is extremely common. Wise and Sulzberger[2] feel that nearly all drug eruptions fall into this category of sensitization reactions.

Dosage does not appear to play a great part, as exceedingly small amounts will produce eruptions in sensitive individuals. Babington[3] reported a patient who developel a toxic eruption the second day after having taken only two one-quarter grain doses of phenobarbital. Other cases have been reported in which large doses, over a considerable length of time, had been given before any cutaneous reaction was noticed.

CUTANEOUS MANIFESTATIONS

The types of cutaneous manifestations seen are: (1) urticarial; (2) erythematous; (3) bullous; (4) eczematous; and (5) fixed.

Urticarial Type.—This is probably the most frequent. The eruption appears immediately, or a few hours after administration of the offending drug. The reaction may be mild, with a few scattered wheals, or may take on the more serious form of angioneurotic edema, with extreme swelling of the affected part. This reaction must be differentiated from urticaria due to some other cause. Stopping of the medication should be followed by a clearing of the condition in a short time, if that is the causative factor.

Erythematous Type.—This form usually appears on the chest and face as brilliant, light-red macules, which may become diffuse if medication is not stopped. If the reaction is severe, the eruption may become universal. This may be followed by a generalized exfoliative dermatitis. Lancaster[4] reported such a case following the taking of phenobarbital. There is nearly always a great deal of pruritus. Edema, particularly about the eyes, is usually part of the picture, and there is an associated conjunctivitis. The mucous membrane of the mouth and the throat may become involved. The mucosa of the rectum and genitalia may also be affected. Frequently there is a slight rise in tem-

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perature. Temperatures of 103 and 104 degrees have been reported. In these cases gastro-intestinal symptoms are usually present. A moderate leukocytosis is present with an increase in eosinophils. These may be as high as 22 per cent. A differential diagnosis must sometimes be made between this type of eruption and scarlet fever or measles. At times this is extremely difficult. A careful history is of importance. The absence of pain and marked injection of the throat would be against scarlet fever. Ordinarily there is not a marked adenopathy with the drug eruption. The tendency of barbiturate eruptions to clear promptly upon withdrawal of the drug is of help. The blanching test for scarlet fever is an aid in distinguishing the two conditions. The absence of Koplik's spots, and the prodromal coryza, would differentiate the drug dermatitis from that of measles.

Bullous Type.—This type is not seen frequently. It is usually associated with the severe erythematous type. The vesicles may vary from miliary size, which are usually transient, to that of large bullae and blebs, simulating pemphigus. The mucous membranes are frequently involved. Weber [5] has reported a case in which there was jaundice along with the bullous eruption. Hemorrhagic bullae also have been described. Following the formation of blebs, extensive ulceration and necrosis have occurred. Mailer [6] reports an interesting case of this kind, in which the reaction was due to nembutal (sodium ethyl—one methyl-butyl—barbiturate). In this case large wheals first appeared on the thighs, followed by vesicles which coalesced into bullae. Necrosis rapidly followed, involving one-half of the anterior portion of the thigh. Similar cases have been seen by Coste and Bolgert,[7] following the use of barbital. The necrotic areas occurred at the sites of pressure appearing as acute decubiti.

Eczematous Type.—Bering [8] recently described a group of five cases in which the clinical picture was that of a papulovesicular eczema. Three of the patients had a primary dermatitis, following the long use of barbiturates. In the other two the eruption was secondary to a chronic pruritic eruption.

Fixed Type.—A fixed eruption is one characterized by recurrences in exactly the same locations. The affected areas usually become pigmented, and at the time of exacerbation are pruritic. This type of reaction, due to several of the barbiturates, has been observed, but is not widely recognized. Wise and Parkhurst,[9] Goldenberg and Rosen,[10] and Fowlkes [11] make mention of this condition caused by these drugs. Loveman [12] published the description of a case following the use of allonal which contains alurate (allylisopropyl-barbituric acid). Langenbach,[13] reporting four cases of dermatitis following the use of sodium amytal (sodium isoamylethyl barbiturate), states that there was some pigmentation, and that in one case, upon repeating the drug, the eruption did occur in the same areas. From his description, however, one cannot be sure that he was dealing with a fixed eruption. I have seen one case in which this type of reaction was found to be due to amytal.

REPORT OF CASE

N. F., female, age thirty, was referred to me for consultation by Dr. C. Cocks. Her chief complaint was recurrent itching patches on the right wrist and left buttock. Examination revealed two circular, sharply circumscribed, hyperpigmented areas of a purple-red hue. The one situated on the dorsum of the right wrist was of dollar-size. The other, on the left buttock, was of palm-size. The rest of the skin was clear. A clinical diagnosis of fixed eruption was made.

The eruption had been present for the past four or five months. It came on suddenly and there was a marked pruritus of the affected areas which lasted several days. The symptoms then cleared. Exacerbations have since occurred at irregular intervals. After each attack the patient noticed that the pigmentation gradually became deeper. Her general health had been good, except for some nervousness and insomnia. For this she had been taking different medicines, including allonal.

The patient was asked to take several tablets of allonal, but no exacerbation took place. Further questioning revealed the fact that, in addition to the allonal she had, on occasion, been taking sleeping capsules that were prescribed for her mother. These were found to be amytal (iso-amyl-ethyl barbituric acid). A few hours after taking one of these capsules, there was a severe exacerbation, with pruritus and deepening of the color of the lesions.

From this observation it was apparent that the exciting factor of this patient's eruption was due to the amytal.

FURTHER OBSERVATIONS

Effect of Other Drugs Producing Fixed Eruptions.—The patient was then instructed to take aspirin and phenolphthalein. Both drugs are known to produce fixed eruptions. There was no reaction. This again confirms similar experiments by Abramowitz [14] and the author [15] on phenolphthalein, and by Loveman [12] on allonal, in which it was shown that an individual with a fixed eruption is not susceptible to all the drugs that cause this type of lesion.

Effect of Taking Other Barbiturates.—She had previously taken allonal with negative results. One-half grain of phenobarbital (phenylethyl-barbituric acid) was given, and there was a definite flare-up of the eruption. Later, when the condition had subsubsided, she was given barbital (diethyl-barbituric acid). Again there was a severe exacerbation, appearing in about twelve hours. As amytal, barbital, and phenobarbital, all contain ethyl-barbituric acid, it was thought that the eruption might be due to this radical. She had not reacted to allonal (allyl-iso-propyl barbituric acid), which does not contain ethylbarbituric acid. Loveman [12] found in his case which reacted to allonal that there was no reaction to the other barbiturates.

Effect of Split Products.—Several split products of barbituric acid were kindly furnished by the Eli Lilly and Company. They were iso-amyl-ethyl malonamid; iso-amyl-ethyl malonic acid; iso-amyl-ethyl acetyl urea; iso-amyl-ethyl acetic acid; iso-amyl-ethyl acetamid. One-half grain doses were administered without reaction. This shows that the eruption was not due to some split product of barbituric acid, which could have been formed in the body.

Patch Tests.—Patch tests were performed in the usual manner with amytal and the split products named above. All were negative. This has been

the usual finding with fixed eruptions. This observation would support the idea that hypersensitiveness in these cases is not in the epidermis and superficial part of the cutis, but is in the deeper layers of the skin.

TREATMENT

These eruptions usually involute rapidly on withdrawal of the offending drug, and no treatment is necessary other than a mild antipruritic, as calamin zinc lotion. Occasionally, in the more severe forms, active treatment is necessary. Johnson[16] and Sanderson[17] have reported good results with the intravenous injection of large amounts of 5 or 10 per cent glucose. A 4 per cent solution of sodium bicarbonate has also been used intravenously when large doses of the barbiturates have been taken.

SUMMARY

Skin eruptions due to the barbiturates are common. Any barbituric acid derivative is capable of producing the different cutaneous reactions which have been described. These reactions are urticarial, erythematous, bullous, eczematous, and fixed.

A case is reported of a fixed eruption due to amytal. Further observations on this patient showed that only the barbiturates with the ethyl-barbituric acid radical would reproduce the eruption.

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DISCUSSION

HARRY E. ALDERSON, M.D. (490 Post Street, San Francisco).—I have seen numerous examples of eruptions due to all the drugs mentioned, excepting amytal. As I prescribe amytal a great deal in small doses, for the relief of pruritus, I may some day see a case of dermatitis medicamentosa due to this drug.

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STANLEY O. CHAMBERS, M.D. (826 Roosevelt Building, Los Angeles).—This particular subject, dealing with drugs so commonly employed in general medicine, seems most apropos. It is appreciated by the author that cutaneous reactions of the common order are familiar to most of us. The intriguing portion of the presentation deals with a fixed eruption. This picture is infrequently identified, and yet relatively common. The discusser has witnessed such lesions about the scrotum and anal region, considered as recurrent scrotal eczema and pruritus ani. These lesions appeared in direct proportion to the ingestion of the drug, and disappeared with its withdrawal. Recurrence was always at the same site. Greater consideration of such possibilities should increase therapeutic effectiveness.

Doctor Novy is to be complimented for his interpretation of such an unfamiliar dermatitis.

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PHILIP K. ALLEN, M.D. (314 Medico-Dental Building, San Diego).—The widespread use of many different barbiturate derivatives and the inevitable intolerance exhibited by some individuals to their use, make the subject an important one.

I think that the fixed eruption is the most interesting type of the drug idiosyncrasies. Its exact place in the field of hypersensitive reactions is still a debatable point. The reaction is not only independent of any circulating antibodies (as shown by the absence of the Prausnitz-Kustner phenomenon), but is confined strictly to certain groups of the fixed tissue cells. Similar tissue outside the reacting areas fails to exhibit the phenomenon, so that cutaneous tests are of little significance except in the areas previously involved.

An interesting feature of Doctor Novy's case is the degree of specificity shown to a certain type of barbiturate derivative. It is frequently of great value to know that a hypersensitivity to one type of drug does not imply that related substances will produce the same reaction.

ACUTE GONORRHEAL ARTHRITIS COMPLICATING PREGNANCY*

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DISCUSSION *by Karl L. Schaupp, M. D., San Francisco; Frances Baker, M. D., San Francisco; William Benbow Thompson, M. D., Los Angeles.*

THE comparative rarity of acute gonorrheal arthritis complicating pregnancy, and the peculiar problems which arise in its treatment during the pregnant state, warrant a consideration of the subject, a review of the literature, and the reporting of a case. The "Index Medicus" for the last ten years contains no articles on this subject.

LITERATURE

Lindermann,[1] in 1892, appears to have been the first man to connect the gonococcus with the resultant complicating arthritis. Jundell,[2] in 1894,

* By permission of the San Francisco Public Health Department, Dr. J. C. Geiger, director.
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